in solution at a given concentration would be comparable using electrospray combined with mass spectrometry at a flow rate of 100 μL/min compared to a flow rate of 100 nL/min. D. C. Gale et al., *Rapid Commun. Mass Spectrom.* 7:1017 (1993) demonstrate that higher electrospray sensitivity is achieved at lower flow rates due to increased analyte ionization efficiency. Thus by performing electrospray on a fluid at flow rates in the nanoliter per minute range provides the best sensitivity for an analyte contained within the fluid when combined with mass spectrometry.

[**0028**] Thus, it is desirable to provide an electrospray device for integration of microchip-based separation devices with API-MS instruments. This integration places a restriction on the capillary tip defining a nozzle on a microchip. This nozzle will, in all embodiments, exist in a planar or near planar geometry with respect to the substrate defining the separation device and/or the electrospray device. When this co-planar or near planar geometry exists, the electric field lines emanating from the tip of the nozzle will not be enhanced if the electric field around the nozzle is not defined and controlled and, therefore, an electrospray is only achievable with the application of relatively high voltages applied to the fluid.

[**0029**] Attempts have been made to manufacture an electrospray device for microchip-based separations. Ramsey et al., *Anal. Chem.* 69:1174-78 (1997) describes a microchip-based separations device coupled with an electrospray mass spectrometer. This separation device is limited by the fact that the separation channels are located on the surface of the substrate, thus limiting the density of an array of such devices. Previous work from this research group including Jacobson et al., *Anal. Chem.* 66:1114-18 (1994) and Jacobson et al., *Anal. Chem.* 66:2369-73 (1994) demonstrate impressive separations using on-chip fluorescence detection. This more recent work demonstrates nanoelectrospray at 90 nL/min from the edge of a planar glass microchip. The microchip-based surface separation channel has dimensions of 10 μm deep, 60 μm wide, and 33 mm in length. Electroosmotic flow is used to generate fluid flow at 90 nL/min. Application of 4,800 V to the fluid exiting the separation channel on the edge of the microchip at a distance of 3-5 mm from the ion-sampling orifice of an API mass spectrometer generates an electrospray. Approximately 12 nL of the sample fluid collects at the edge of the microchip before the formation of a Taylor cone and stable nanoelectrospray from the edge of the microchip. The volume of this microchip-based separation channel is 19.8 nL. Nanoelectrospray from the edge of this microchip device after capillary electrophoresis or capillary electrochromatography separation is rendered impractical since this system has a dead-volume approaching 60% of the column (channel) volume. Furthermore, because this device provides a flat surface, and, thus, a relatively small amount of physical asperity for the formation of the electrospray, the device requires an impractically high voltage to overcome the fluid surface tension to initiate an electrospray.

[**0030**] Xue, Q. et al., *Anal. Chem.* 69:426-30 (1997) also describes a stable nanoelectrospray from the edge of a planar glass microchip with a closed channel 25 μm deep, 60 μm wide, and 35-50 mm in length. An electrospray is formed by applying 4,200 V to the fluid exiting the separation channel on the edge of the microchip at a distance of 3-8 mm from the ion-sampling orifice of an API mass spectrometer. A syringe pump is utilized to deliver the sample fluid to the glass microchip at a flow rate of 100 to 200 nL/min. The edge of the glass microchip is treated with a hydrophobic coating to alleviate some of the difficulties associated with nanoelectrospray from a flat surface that slightly improves the stability of the nanoelectrospray. Nevertheless, the volume of the Taylor cone on the edge of the microchip is too large relative to the volume of the separation channel, making this method of electrospray directly from the edge of a microchip impracticable when combined with a chromatographic separation device.

[**0031**] T. D. Lee et. al., 1997 *International Conference on Solid-State Sensors* and Actuators Chicago, pp. 927-30 (Jun. 16-19, 1997) describes a multi-step process to generate a nozzle on the edge of a silicon microchip 1-3 μm in diameter or width and 40 μm in length and applying 4,000 V to the entire microchip at a distance of 0.25-0.4 mm from the ion-sampling orifice of an API mass spectrometer. Because a relatively high voltage is required to form an electrospray with the nozzle positioned in very close proximity to the mass spectrometer ion-sampling orifice, this device produces an inefficient electrospray that does not allow for sufficient droplet evaporation before the ions enter the orifice. The extension of the nozzle from the edge of the microchip also exposes the nozzle to accidental breakage. More recently, T. D. Lee et.al., in 1999 *Twelfth IEEE International Micro Electro Mechanical Systems Conference (Jan.* 17-21, 1999), presented this same concept where the electrospray component was fabricated to extend 2.5 mm beyond the edge of the microchip to overcome this phenomenon of poor electric field control within the proximity of a surface.

[**0032**] Thus, it is also desirable to provide an electrospray device with controllable spraying and a method for producing such a device that is easily reproducible and manufacturable in high volumes.

[**0033**] U.S. Pat. No. 5,501,893 to Laermer et. al., reports a method of anisotropic plasma etching of silicon (Bosch process) that provides a method of producing deep vertical structures that is easily reproducible and controllable. This method of anisotropic plasma etching of silicon incorporates a two step process. Step one is an anisotropic etch step using a reactive ion etching (RIE) gas plasma of sulfur hexafluoride (SF_6). Step two is a passivation step that deposits a polymer on the vertical surfaces of the silicon substrate. This polymerizing step provides an etch stop on the vertical surface that was exposed in step one. This two step cycle of etch and passivation is repeated until the depth of the desired structure is achieved. This method of anisotropic plasma etching provides etch rates over 3 μm/min of silicon depending on the size of the feature being etched. The process also provides selectivity to etching silicon versus silicon dioxide or resist of greater than 100:1 which is important when deep silicon structures are desired. Laermer et. al., in 1999 *Twelfth IEEE International Micro Electro Mechanical Systems Conference (Jan.* 17-21, 1999), reported improvements to the Bosch process. These improvements include silicon etch rates approaching 10 μm/min, selectivity exceeding 300:1 to silicon dioxide masks, and more uniform etch rates for features that vary in size.

[**0034**] The study of expressed proteins within an organism or specific cell type is known as proteomics. The study of a